

PATENT COOPERATION TREATY

PCT

**NOTIFICATION CONCERNING
SUBMISSION OR TRANSMITTAL
OF PRIORITY DOCUMENT**

(PCT Administrative Instructions, Section 411)

From the INTERNATIONAL BUREAU

To:

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Italy

Date of mailing (day/month/year) 16 July 2003 (16.07.03)			
Applicant's or agent's file reference PCT30112	IMPORTANT NOTIFICATION		
International application No. PCT/IT03/00265	International filing date (day/month/year) 29 April 2003 (29.04.03)		
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 03 July 2002 (03.07.02)		
<p>Applicant</p> <p>FONDAZIONE CENTRO SAN RAFFAELE DEL MONTE TABOR et al</p>			
<p>1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).</p> <p>2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.</p> <p>3. An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.</p> <p>4. The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.</p>			
<u>Priority date</u> 03 July 2002 (03.07.02)	<u>Priority application No.</u> 60/393,994	<u>Country or regional Office or PCT receiving Office</u> US	<u>Date of receipt of priority document</u> 15 July 2003 (15.07.03)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 740-1435	Authorized officer Zakaria EL KHODARY Telephone No. (41-22) 338 8240
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PATENT COOPERATION TREATY

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference PCT30112	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, Item 5 below.	
International application No. PCT/ IT 03/ 00265	International filing date (day/month/year) 29/04/2003	(Earliest) Priority Date (day/month/year) 03/07/2002
Applicant CENTRO CARDIOLOGICO MONZINO S.P.A. IRCCS		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

contained in the international application in written form.

filed together with the international application in computer readable form.

furnished subsequently to this Authority in written form.

furnished subsequently to this Authority in computer readable form.

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. Certain claims were found unsearchable (See Box I).

3. Unity of invention is lacking (see Box II).

4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

as suggested by the applicant.

because the applicant failed to suggest a figure.

because this figure better characterizes the invention.

None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IT 03/00265

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K16/18 A61K39/395 A61P9/10 A61P29/00 C07K14/47
A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, MEDLINE, WPI Data, PAJ, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category ^o	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 47104 A (PICOWER INST MED RES) 17 August 2000 (2000-08-17) page 3, line 19 - line 37 page 6, line 16 - line 38 page 10, line 27 -page 11, line 9 page 11, line 10 - line 22 example 6 ---	11-15
X	WO 01 89526 A (NORTH SHORE LONG ISLAND JEWISH) 29 November 2001 (2001-11-29) page 2, line 8,12,13,25 page 32; example 4 --- -/-	11-14

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the International search	Date of mailing of the International search report
13 November 2003	19/12/2003
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Fax: (+31-70) 340-3016	Authorized officer Irion, A

INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FANG WEN-HUI ET AL: "The significance of changes in high mobility group-1 protein mRNA expression in rats after thermal injury." SHOCK (AUGUSTA, GA.) UNITED STATES APR 2002, vol. 17, no. 4, April 2002 (2002-04), pages 329-333, XP009020804 ISSN: 1073-2322 abstract ---	11,13,14 D3
X	FAGES C ET AL: "REGULATION OF CELL MIGRATION BY AMPHOTERIN" JOURNAL OF CELL SCIENCE, ESSEX, GB, vol. 113, no. 4, February 2000 (2000-02), pages 611-620, XP001070170 abstract ---	16-18 D4
X	MULLER SUSANNE ET AL: "The double life of HMGB1 chromatin protein: Architectural factor and extracellular signal" EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 20, no. 16, 15 August 2001 (2001-08-15), pages 4337-4340, XP002261324 ISSN: 0261-4189 page 4338, right-hand column, paragraph 3 - paragraph 4 ---	16-18 D5
X	WANG HAICHAO ET AL: "HMGB1 as a late mediator of lethal systemic inflammation" AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE, vol. 164, no. 10 Part 1, 15 November 2001 (2001-11-15), pages 1768-1773, XP002261325 ISSN: 1073-449X the whole document ---	11-15 D6
X	WANG H ET AL: "HMG-1 AS A LATE MEDIATOR OF ENDOTOXIN LETHALITY IN MICE" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, US, vol. 285, 9 July 1999 (1999-07-09), pages 248-251, XP002940163 ISSN: 0036-8075 cited in the application the whole document --- -/-	11-15 D7

INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 02 092004 A (GEN HOSPITAL CORP ;YANG HUAN (US); FINK MITCHELL P (US); TRACEY KE) 21 November 2002 (2002-11-21) page 3, line 20 - line 30 page 6, line 8 - line 22 page 7, line 1 - line 6 page 8, line 3 - line 7 page 14, line 15 - line 17 page 13, line 1 - line 7 page 16, line 1 - line 3 page 23, line 5,6,15,17 page 28, line 6 - line 10 page 31, line 4 - line 8 page 30, line 19 - line 20 examples 5-7,12,13 ---	1-18
P, X	WO 02 074301 A (FINK MITCHELL P ;TRACEY KEVIN J (US); ULLOA LUIS (US); UNIV PITTSB) 26 September 2002 (2002-09-26) the whole document ---	11-15
P, X	YANG HUAN ET AL: "HMGB1 as a cytokine and therapeutic target." JOURNAL OF ENDOTOXIN RESEARCH, vol. 8, no. 6, 2002, pages 469-472, XP009020930 ISSN: 0968-0519 the whole document ---	11-14
P, X	SCAFFIDI PAOLA ET AL: "Release of chromatin protein HMGB1 by necrotic cells triggers inflammation" NATURE (LONDON), vol. 418, no. 6894, 11 July 2002 (2002-07-11), pages 191-195, XP002261326 ISSN: 0028-0836 the whole document ---	11-15
A	WO 97 23611 A (BULLERDIEK JOERN) 3 July 1997 (1997-07-03) abstract page 21, line 24 - line 31 page 20, line 29 - line 36 page 12, line 52 - line 53 page 11, line 57 - line 65 page 10, line 33 - line 34 page 5, line 53 - line 55 --- -/-	1-10, 16-18

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>YANG R ET AL: "ETHYL PYRUVATE MODULATES INFLAMMATORY GENE EXPRESSION IN MICE SUBJECTED TO HEMORRHAGIC SHOCK" AMERICAN JOURNAL OF PHYSIOLOGY: GASTROINTESTINAL AND LIVER PHYSIOLOGY, AMERICAN PHYSIOLOGICAL SOCIETY, US, vol. 283, 2002, pages G212-G221, XP008019310 ISSN: 0193-1857</p> <p>---</p>	DB
A	<p>SIMS C A ET AL: "RINGER'S ETHYL PYRUVATE SOLUTION AMELIORATES ISCHEMIA/REPERFUSION-INDUCED INTESTINAL MUCOSAL INJURY IN RATS" CRITICAL CARE MEDICINE, WILLIAMS AND WILKINGS COMPANY, BALTIMORE, MA, US, vol. 29, no. 8, 2001, pages 1513-1518, XP008019328 ISSN: 0090-3493</p> <p>-----</p>	D4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IT 03/00265

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 16-18 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

/IT 03/00265

Patent document cited in search report	Publication date		Patent family member(s)		Publication date
WO 0047104	A	17-08-2000	US 6303321 B1 AU 3698300 A CA 2359926 A1 EP 1165110 A2 JP 2003520763 T WO 0047104 A2 US 2003017155 A1 US 2003113323 A1 US 2003143194 A1 US 6468533 B1 US 2002102609 A1		16-10-2001 29-08-2000 17-08-2000 02-01-2002 08-07-2003 17-08-2000 23-01-2003 19-06-2003 31-07-2003 22-10-2002 01-08-2002
WO 0189526	A	29-11-2001	US 2002016344 A1 AU 6162901 A CA 2408791 A1 EP 1307196 A1 WO 0189526 A1		07-02-2002 03-12-2001 29-11-2001 07-05-2003 29-11-2001
WO 02092004	A	21-11-2002	WO 02092004 A2 US 2003060410 A1 US 2003144201 A1		21-11-2002 27-03-2003 31-07-2003
WO 02074301	A	26-09-2002	WO 02074301 A1		26-09-2002
WO 9723611	A	03-07-1997	DE 19548122 A1 AU 1870597 A CA 2239682 A1 WO 9723611 A2 EP 0870024 A2 JP 2000504933 T NZ 504445 A US 6323329 B1 US 2002120120 A1		26-06-1997 17-07-1997 03-07-1997 03-07-1997 14-10-1998 25-04-2000 28-08-2002 27-11-2001 29-08-2002